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It is believed that no additional fee is required with this submission. However, should a additional fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-1868.

Amendment

In the Specification

Please replace the paragraph on page 24, lines 1-8, with the following paragraph.

-The nucleic acid vaccine may be administered without adjuvant. The nucleic acid vaccine may also be administered with an adjuvant such as BCG or alum. Other suitable adjuvants include Aquila's QS21 [stimulon] STIMULON™ (Aquila Biotech, Worcester, MA, USA) which is derived from saponin, mycobacterial extracts and synthetic bacterial cell wall mimics, and proprietory adjuvants such as Ribi's [Detox] DETOX™. Quil A, another saponin-derived adjuvant, may also be used (Superfos, Denmark). It is preferred if the nucleic acid vaccine is administered without adjuvant.-

Please replace the paragraph bridging pages 20 and 21 with the following paragraph.

-The peptide or peptide-encoding nucleic acid constitutes a tumour or cancer vaccine. It may be administered directly into the patient, into the affected organ or systemically, or applied *ex vivo* to cells derived from the patient or a human cell line which are subsequently administered to the patient, or used *in vitro* to select a subpopulation from immune cells derived

from the patient, which are then re-administered to the patient. If the nucleic acid is administered to cells *in vitro*, it may be useful for the cells to be transfected so as to co-express immune-stimulating cytokines, such as interleukin-2. The peptide may be substantially pure, or combined with an immune-stimulating adjuvant such as [Detox] DETOX™, or used in combination with immune-stimulatory cytokines, or be administered with a suitable delivery system, for example liposomes. The peptide may also be conjugated to a suitable carrier such as keyhole limpet haemocyanin (KLH) or mannan (see WO 95/18145 and Logenecker *et al.* (1993) Ann. NY Acad. Sci., 690, 276-291). The peptide may also be tagged, or be a fusion protein, or be a hybrid molecule. The peptides whose sequence is given in the first or second or third aspects of the invention are expected to stimulate CD8 CTL. However, stimulation is more efficient in the presence of help provided by CD4 T cells. Thus, the fusion partner or sections of a hybrid molecule suitably provide epitopes which stimulate CD4 T cells. CD4 stimulating epitopes are well known in the art and include those identified in tetanus toxoid. The polynucleotide may be substantially pure, or contained in a suitable vector or delivery system. Suitable vectors and delivery systems include viral, such as systems based on adenovirus, vaccinia virus, retroviruses, herpes virus, adeno-associated virus or hybrids containing elements of more than one virus. Non-viral delivery systems include cationic lipids and cationic polymers as are well known in the art of DNA delivery. Physical delivery, such as *via* a "gene-gun" may also be used. The peptide or peptide encoded by the nucleic acid may be a fusion protein, for example with an epitope from tetanus toxoid which stimulates CD4 T cells.

U.S.S.N. 09/625,963
Filed: July 26, 2000
CLEAN VERSION OF AMENDMENTS PURSUANT TO 37 C.F.R. § 1.121

Clean Version of Amended Specification Paragraphs
Pursuant to 37 C.F.R. § 1.121(b)(1)(iii)

Please replace the paragraph on page 24, lines 1-8, with the following paragraph.

The nucleic acid vaccine may be administered without adjuvant. The nucleic acid vaccine may also be administered with an adjuvant such as BCG or alum. Other suitable adjuvants include Aquila's QS21 STIMULON™ (Aquila Biotech, Worcester, MA, USA) which is derived from saponin, mycobacterial extracts and synthetic bacterial cell wall mimics, and proprietory adjuvants such as Ribi's DETOX™. Quil A, another saponin-derived adjuvant, may also be used (Superfos, Denmark). It is preferred if the nucleic acid vaccine is administered without adjuvant.

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haemocyanin (KLH) or mannan (see WO 95/18145 and Logenecker *et al.* (1993) Ann. NY Acad. Sci., 690, 276-291). The peptide may also be tagged, or be a fusion protein, or be a hybrid molecule. The peptides whose sequence is given in the first or second or third aspects of the invention are expected to stimulate CD8 CTL. However, stimulation is more efficient in the presence of help provided by CD4 T cells. Thus, the fusion partner or sections of a hybrid molecule suitably provide epitopes which stimulate CD4 T cells. CD4 stimulating epitopes are well known in the art and include those identified in tetanus toxoid. The polynucleotide may be substantially pure, or contained in a suitable vector or delivery system. Suitable vectors and delivery systems include viral, such as systems based on adenovirus, vaccinia virus, retroviruses, herpes virus, adeno-associated virus or hybrids containing elements of more than one virus. Non-viral delivery systems include cationic lipids and cationic polymers as are well known in the art of DNA delivery. Physical delivery, such as *via* a "gene-gun" may also be used. The peptide or peptide encoded by the nucleic acid may be a fusion protein, for example with an epitope from tetanus toxoid which stimulates CD4 T cells.--

ATL1 #509304 v1

U.S.S.N. 09/625,963
Filed: July 26, 2000
MARKED UP VERSION OF AMENDMENTS PURSUANT TO 37 C.F.R. § 1.121

Marked Up Version of Amended Specification Paragraphs
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